

EXHIBIT 29

Influenza Surveillance Report

2019–2020 Season

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Center for Infectious Diseases
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Table of Contents

Synopsis	1
Surveillance Data	3
A. CDPH Virologic Surveillance	3
1. Respiratory Laboratory Network (RLN) Surveillance	4
2. Clinical Sentinel Laboratory Surveillance	6
3. Influenza Virus Characterization	11
4. Antiviral Resistance Testing	13
5. Novel Influenza A Viruses.....	14
B. Case-Based Surveillance	14
1. Influenza-associated Pediatric Deaths	14
2. California Emerging Infections Program Data: Influenza-associated Hospitalizations	15
C. Syndromic Surveillance.....	17
1. Influenza-like Illness Outpatient Surveillance (Sentinel Providers)	17
2. Kaiser Permanente Northern California Pneumonia and Influenza Admission Data	20
3. Influenza Mortality Surveillance from Death Certificates	24
D. Outbreaks of Respiratory Illness, Including Influenza.....	27
References	29

Notes: This report will primarily focus on influenza surveillance in California; however, information on other non-SARS-CoV-2 respiratory viruses is provided where data are available. The majority of data in this report covers the influenza season (September 29, 2019–May 16, 2020 [calendar weeks 2019-40 – 2020-20]); however, some data sources cover the period September 29, 2019–September 26, 2020 (calendar weeks 2019-40 – 2020-39). Data presented in this report are as of December 12, 2020; any deviations from this are noted where applicable.

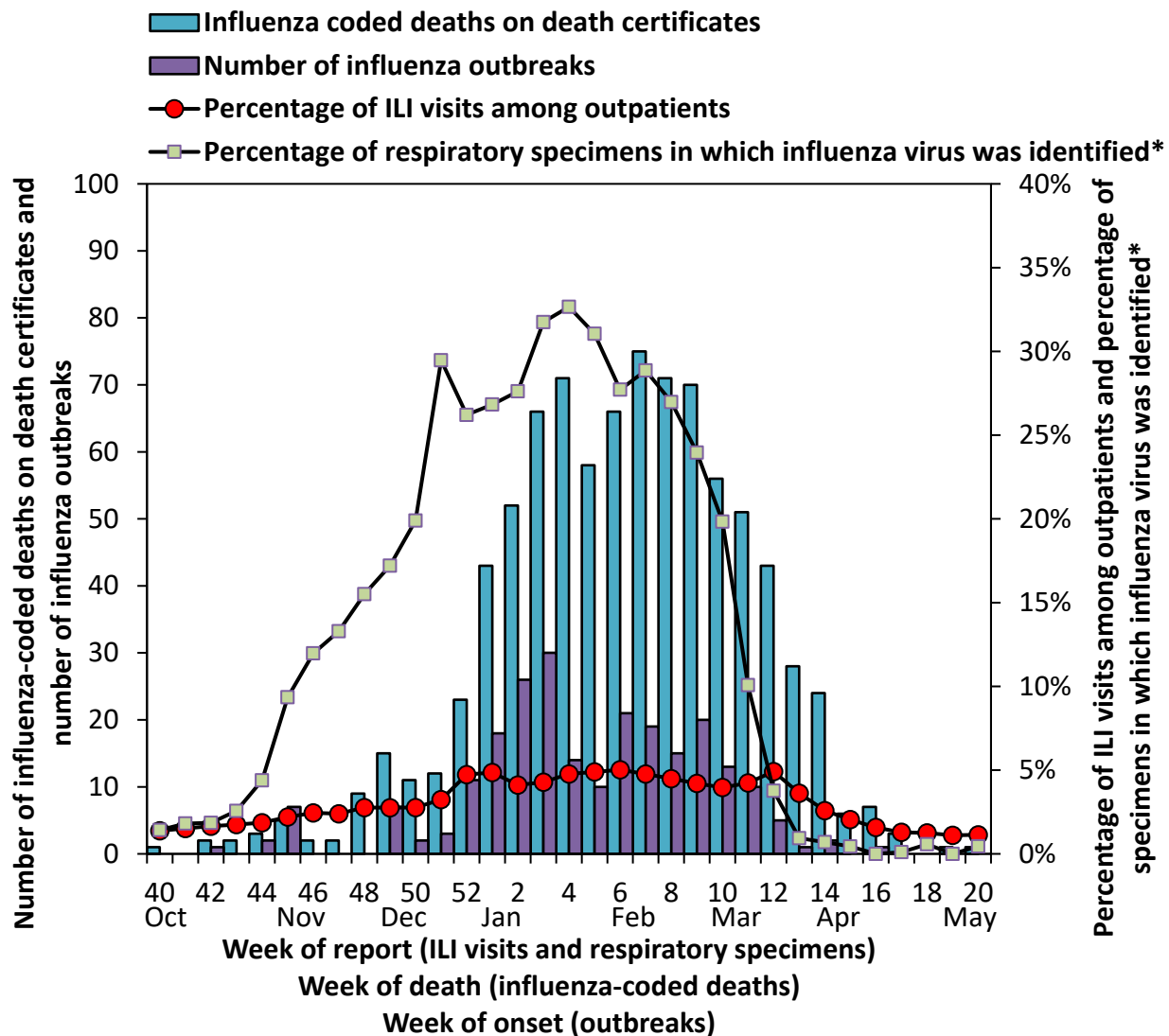
Important: An accessible excel file with data for all figures can be downloaded from the [CDPH flu webpage](#).

Synopsis

- National influenza activity^{1,2}
 - Influenza-like illness (ILI) activity began increasing in November, had three peaks occurring in late December (7.1%), early February (6.8%), and mid-March (6.4%), and returned to baseline in mid-April.
 - The first peak in ILI activity coincided with a peak in influenza B activity and increasing influenza A activity.
 - The second peak in ILI activity coincided with a peak in influenza A activity and continuing circulation of influenza B viruses.
 - The third peak in ILI activity coincided with increasing SARS-CoV-2 circulation and rapidly declining influenza A and B activity.
 - ILI activity remained above baseline levels for 23 weeks.
 - Both influenza A and B circulated during the 2019–2020 influenza season; influenza B (Victoria) viruses predominated from October 2019 to early January 2020 and influenza A(H1N1)pdm09 viruses from late January through March 2020, when influenza activity declined to inter-seasonal levels.
- California influenza activity
 - Summary
 - Overall influenza activity was high in severity.
 - High severity levels of hospitalizations for influenza at Northern Kaiser Permanente facilities and influenza-coded deaths on death certificates.
 - However, outpatient visits for ILI and hospitalizations for pneumonia and influenza at Northern Kaiser Permanente facilities remained within moderate severity levels.
 - Influenza activity began increasing in November, reached an initial peak in late December, and a secondary peak in late January, before returning to baseline levels in late March (Figure 1).
 - Syndromic surveillance systems used for influenza surveillance also identified a third peak in activity during late March that coincided with increasing SARS-CoV-2 circulation in California.³
 - Influenza B (Victoria) viruses predominated early in the season; however influenza A (H1N1)pdm09 viruses predominated during the second half of the season. Very few influenza A (H3N2) viruses were identified.
 - Duration of this season was similar to that of the 2017–2018 and 2018–2019 influenza seasons, which all had several more weeks of elevated influenza activity compared to the 2015–2016 and 2016–2017 influenza seasons.
 - Outpatient influenza-like illness activity
 - Percentage of ILI visits among outpatients had three periods of peak activity in California.

- First peak occurred during the week ending January 4, 2020 (4.9%), corresponding to a period when influenza B (Victoria) activity was near its peak and influenza A (H1N1)pdm09 activity was increasing.
- Second peak occurred during the week ending February 8, 2020 (5.0%), corresponding to the period when influenza A (H1N1)pdm09 activity was peaking and influenza B (Victoria) activity was still elevated.
- Third peak occurred during the week ending March 21, 2020 (4.9%), corresponding to a period of sharp decline in influenza activity, but coinciding with increases in awareness and community transmission of SARS-CoV-2, the virus that cause COVID-19.
- Laboratory surveillance for influenza
 - Percentage of specimens testing positive for influenza at sentinel clinical laboratories in California began increasing in November
 - Period of sustained elevated activity between the week ending December 21, 2019 and the week ending February 29, 2020, during which more than 20% of specimens tested positive for influenza.
 - Peak of 32.7% during the week ending January 25, 2020.
 - Remained elevated through the week ending March 14, 2020, after which the percentage of specimens testing positive for influenza declined below 10%.
- Influenza outbreaks
 - 279 confirmed respiratory outbreaks were reported during the 2019–2020 season; 238 were associated with influenza.
 - Among the 238 influenza-associated outbreaks, influenza A was the most commonly identified influenza virus.
 - Majority of influenza-associated outbreaks occurred in residential healthcare facilities; however, outbreaks occurring in residential healthcare facilities are more likely to be identified and reported to CDPH than other respiratory outbreaks.
- Influenza-associated pediatric deaths
 - 22 laboratory-confirmed influenza-associated pediatric deaths were reported to the California Department of Public Health (CDPH) during September 29, 2019–September 26, 2020.
 - Within range of previous influenza season reported pediatric deaths since fatal pediatric influenza surveillance began in 2003.
 - Minimum: 5 during the 2007–2008 season.
 - Maximum: 37 during the 2008–2009 season.
- Influenza-coded deaths on death certificates
 - 889 influenza coded deaths were identified on death certificates compared to 613 identified in 2018–2019.

Figure 1. Selected influenza surveillance parameters, California Department of Public Health, 2019–2020



*Specimens tested at clinical sentinel laboratories only

Surveillance Data

A. CDPH Virologic Surveillance

The CDPH obtains data on laboratory-confirmed influenza and other respiratory viruses from laboratories throughout the state. These laboratories include the CDPH Viral and Rickettsial Disease Laboratory (VRDL) and 22 local public health laboratories, collectively known as the Respiratory Laboratory Network (RLN), and 16 clinical, academic, and hospital laboratories, which are referred to as clinical sentinel laboratories.

During the 2019–2020 influenza season, influenza A viruses were the influenza viruses most commonly identified by RLN and clinical sentinel laboratories; however, influenza B viruses also circulated widely. Influenza B (Victoria) viruses predominated through early January. Influenza A

(H1N1)pdm09 virus activity began increasing in late December and became the predominant circulating influenza virus in January (Figure 2). Very few influenza A (H3N2) and influenza B (Yamagata) viruses were identified during the 2019–2020 influenza season. These virologic surveillance data are similar to national findings.¹

The proportion of specimens testing positive at clinical sentinel laboratories for all types of influenza first exceeded 10% – an indication that higher than normal levels of influenza virus were circulating – during the week ending November 16, 2019 (Figure 3). The proportion of influenza-positive specimens peaked at 32.7% during the week ending January 25, 2020; however, a sustained level of elevated activity occurred during the week ending December 21, 2019 (29.5% of specimens tested positive for influenza) through the week ending February 29, 2020 (24.0% of specimens tested positive for influenza). Activity declined to less than 10% during the week ending March 21, 2020. National influenza activity also peaked during both the week ending December 28, 2019 (26.9%) and the week ending February 8, 2020 (30.3%), corresponding to peak activity for influenza B and influenza A viruses, respectively.¹

1. Respiratory Laboratory Network (RLN) Surveillance

The RLN laboratories offer polymerase chain reaction (PCR) testing for influenza A and influenza B, including influenza A subtyping and influenza B lineage typing, and some offer testing for respiratory syncytial virus (RSV), a common respiratory virus. RLN laboratories often receive specimens that have already tested positive for influenza at a clinical laboratory; therefore, the percentage of specimens testing positive for influenza at RLN laboratories is not an accurate indicator of influenza activity.

Of 9,824 specimens tested by RLN laboratories from September 29, 2019–May 16, 2020, 5,687 (57.9%) were positive for influenza; of these, 3,452 (60.7%) were influenza A and 2,235 (39.3%) were influenza B (Table 1). Of the 3,452 positive influenza A specimens, 2,994 (86.7%) were A (H1N1)pdm09, 268 (7.8%) were A (H3N2), and 190 (5.5%) were not subtyped. Of the 2,235 positive influenza B specimens, 36 (1.6%) were B/Yamagata lineage, 1,745 (78.1%) were B/Victoria lineage, and 454 (20.3%) were not lineage typed. In addition to influenza testing, 1,424 specimens were tested for RSV by RLN laboratories; 125 (8.8%) were positive.

Table 1. RLN* influenza and respiratory syncytial virus (RSV) surveillance results, September 29, 2019–May 16, 2020

	Total No.	Total %	Northern No.	Northern %	Bay Area No.	Bay Area %	Central No.	Central %	Upper Southern No.	Upper Southern %	Lower Southern No.	Lower Southern %
Specimens tested for influenza	9,824		783		3,060		1,127		3,113		1,741	
Positive for influenza	5,687	57.9 [†]	524	66.9 [†]	1,687	55.1 [†]	710	63.0 [†]	1,580	50.8 [†]	1,186	68.1 [†]
Influenza A	3,452	60.7 [‡]	240	45.8 [‡]	1,257	74.5 [‡]	467	65.8 [‡]	781	49.4 [‡]	707	59.6 [‡]
<i>A (H1N1)pdm09</i>	2,994	86.7 [§]	216	90.0 [§]	1,128	89.7 [§]	405	86.7 [§]	662	84.8 [§]	583	82.5 [§]
<i>A (H3N2)</i>	268	7.8 [§]	10	4.2 [§]	69	5.5 [§]	41	8.8 [§]	44	5.6 [§]	104	14.7 [§]
<i>Subtyping not performed</i>	190	5.5 [§]	14	5.8 [§]	60	4.8 [§]	21	4.5 [§]	75	9.6 [§]	20	2.8 [§]
Influenza B	2,235	39.3 [‡]	284	54.2 [‡]	430	25.5 [‡]	243	34.2 [‡]	799	50.6 [‡]	479	40.4 [‡]
<i>Yamagata</i>	36	1.6 ^{**}	12	4.2 ^{**}	7	1.6 ^{**}	0	0.0 ^{**}	3	0.4 ^{**}	14	2.9 ^{**}
<i>Victoria</i>	1,745	78.1 ^{**}	265	93.3 ^{**}	368	85.6 ^{**}	11	4.5 ^{**}	664	83.1 ^{**}	437	91.2 ^{**}
<i>Lineage typing not performed</i>	454	20.3 ^{**}	7	2.5 ^{**}	55	12.8 ^{**}	232	95.5 ^{**}	132	16.5 ^{**}	28	5.8 ^{**}
Specimens tested for RSV	1,424		49		903		303		1		168	
Positive for RSV	125	8.8	10	20.4	81	9.0	23	7.6	0	0.0	11	6.5

* Participating laboratories – Statewide: CDPH Viral and Rickettsial Disease Laboratory; Northern: Humboldt, Sacramento, and Shasta county public health laboratories (PHLs); Bay Area: Alameda, Contra Costa, San Francisco, San Mateo, Santa Clara, Solano, and Sonoma county PHLs; Central: Monterey, San Joaquin, and Tulare county PHLs; Upper Southern: Long Beach, Los Angeles, San Luis Obispo, Santa Barbara, and Ventura county PHLs; Lower Southern: Orange, Riverside, San Bernardino, and San Diego county PHLs

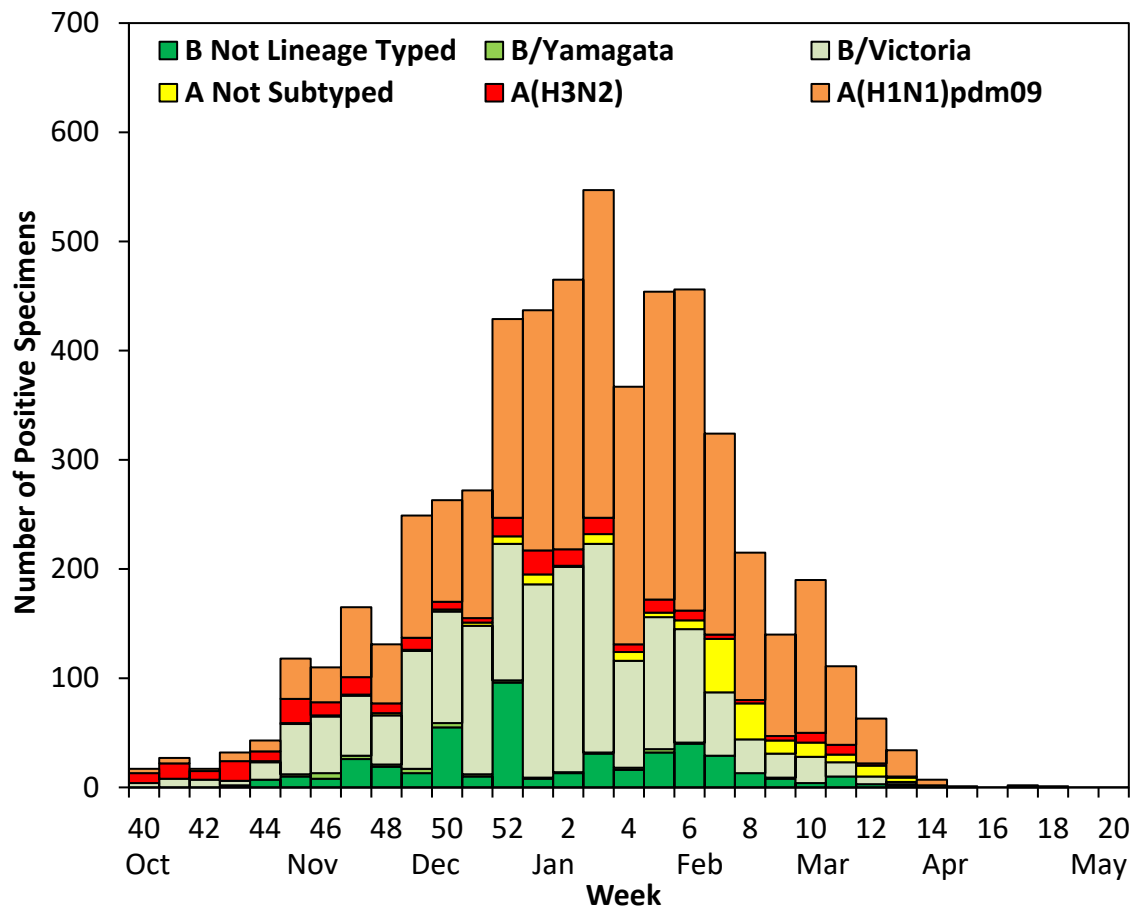
[†] Percent is of the total specimens tested for influenza by PCR

[‡] Percent is of the specimens positive for influenza

[§] Percent is of the influenza A positive specimens

^{**} Percent is of the influenza B positive specimens

Figure 2. Influenza positive specimens by type and subtype, Respiratory Laboratory Network Laboratories, 2019–2020



2. Clinical Sentinel Laboratory Surveillance

The clinical sentinel laboratories use various methods to test for influenza, including rapid test, direct fluorescent assay, viral culture, and PCR. Because clinical sentinel laboratory specimens submitted for influenza testing are collected from patients in healthcare settings, they are more likely to reflect influenza activity than specimens tested at RLN laboratories; however, many clinical laboratories do not perform influenza A subtyping or influenza B lineage typing.

From September 29, 2019 through May 16, 2020, clinical sentinel laboratories tested 122,362 specimens for influenza, of which 24,211 (19.8%) were positive for influenza. Of the 24,211 specimens that tested positive, 14,214 (58.7%) were positive for influenza A and 9,997 (41.3%) were positive for influenza B (Table 2). In addition, clinical sentinel laboratories tested 106,934 specimens for RSV, of which 9,057 (8.5%) were positive.

During the 2019–2020 season, influenza activity reported by clinical laboratories exceeded 10% of specimens testing positive for 18 weeks, including a sustained period of elevated activity for 11 weeks between the week ending December 21, 2019 and the week ending February 29, 2020 during which more than 20% of specimens tested positive for influenza (Figure 3). Peak weeks of influenza activity varied by region (Figure 4). Peaks in activity were experienced in the Upper Southern region during the week ending January 4, 2019, the Bay Area and Northern regions during the week ending January 25, 2020, and the Central region during the week ending

February 1, 2020. The Lower Southern region had a less clearly defined peak week of activity, but did experience an extended period of elevated influenza activity during the weeks ending November 30, 2019 through February 15, 2020 where the percentage of specimens tested that were positive for influenza plateaued between 25% and 31%. The percentage of specimens testing positive for influenza sharply decreased in all regions in late February and early March, when COVID-19 activity and testing capacity in California began to increase.

The percentage of specimens testing positive for RSV plateaued between 12.1% and 13.6% for 9 weeks between the week ending December 28, 2019 and the week ending February 22, 2020, which coincided with peak influenza activity (Figure 5). Rhinoviruses and enteroviruses were the most frequently detected viruses among other tested respiratory viruses; however, decreases in activity were seen for all respiratory viruses beginning in late March 2020 (Figure 6). This corresponded to increases in activity of COVID-19.³

Table 2. Influenza and respiratory syncytial virus (RSV) detections in clinical sentinel laboratories*, September 29, 2019–May 16, 2020

	Total No.	Total %	Northern No.	Northern %	Bay Area No.	Bay Area %	Central No.	Central %	Upper Southern No.	Upper Southern %	Lower Southern No.	Lower Southern %
Influenza												
Specimens tested	122,362		10,279		37,528		12,816		27,894		16,484	
Positive for influenza	24,211	19.8 [†]	2,763	26.9 [†]	9,583	25.5 [†]	3,672	28.7 [†]	3,475	12.5 [†]	3,338	20.2 [†]
Influenza A	14,214	58.7 [‡]	1,761	63.7 [‡]	5,965	62.2 [‡]	1,782	48.5 [‡]	2,090	60.1 [‡]	1,832	54.9 [‡]
Influenza B	9,997	41.3 [‡]	1,002	36.3 [‡]	3,618	37.8 [‡]	1,890	51.5 [‡]	1,385	39.9 [‡]	1,506	45.1 [‡]
RSV												
Specimens tested	106,934		8,168		37,528		9,291		25,588		8,998	
Positive for RSV	9,057	8.5	798	9.8	3,168	8.4	1,201	12.9	1,806	7.1	1,186	13.2

* Number of participating laboratories by region and county:

Northern: Butte (1). In addition, Northern California Kaiser Permanente has facilities in multiple counties within the Northern California region.

Bay Area: Alameda (1), Marin (1), and San Francisco (1). In addition, Northern California Kaiser Permanente has facilities in multiple counties within the Bay Area region.

Central: Madera (1). In addition, Northern California Kaiser Permanente has facilities in multiple counties within the Central California region.

Upper Southern: Long Beach (1) and Los Angeles (3).

Lower Southern: Imperial (3) and San Diego (2).

In addition, Southern California Kaiser Permanente provides aggregated data for all their facilities, which are located in multiple counties within the Upper Southern and Lower Southern regions; therefore, Southern California Kaiser Permanente data are included in the total but not in the Upper Southern and Lower Southern region columns.

[†] Percent is of the total specimens tested for influenza

[‡] Percent is of the specimens positive for influenza

Figure 3. Percentage of specimens from which influenza was detected in clinical sentinel laboratories, 2015–2020

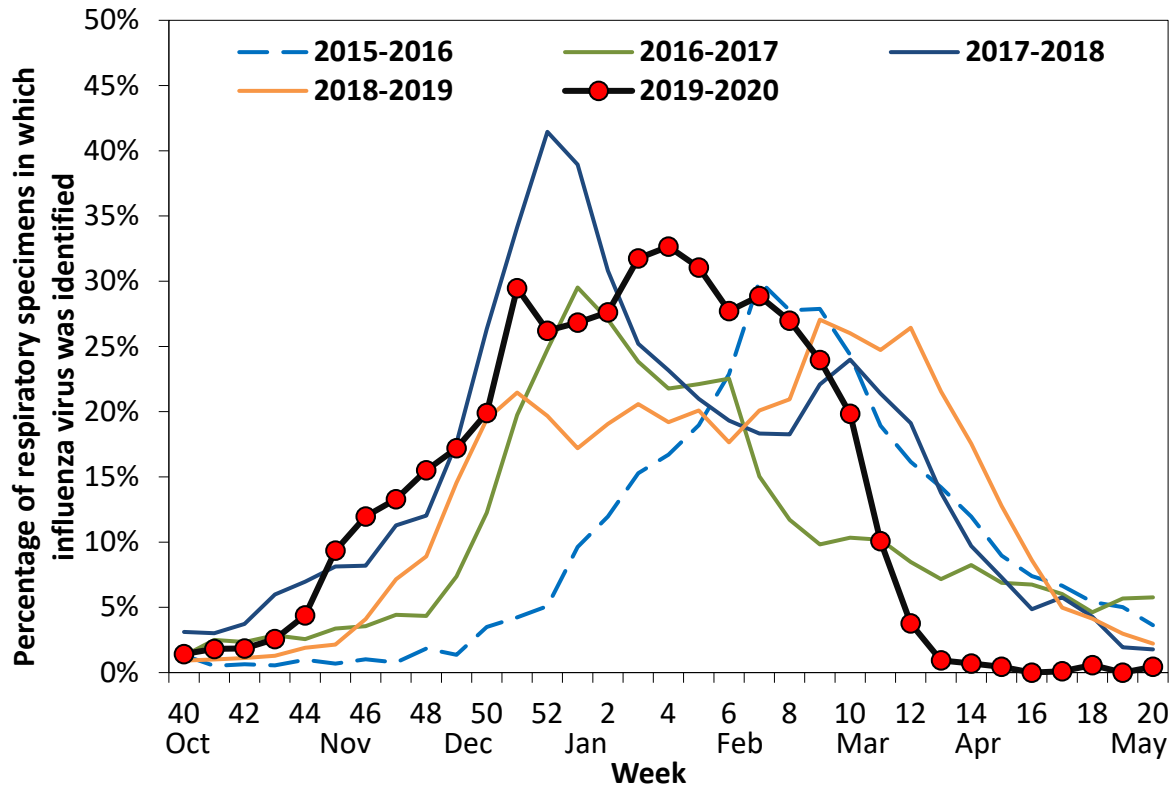


Figure 4. Percentage of specimens from which influenza was detected in clinical sentinel laboratories by California region, 2019–2020

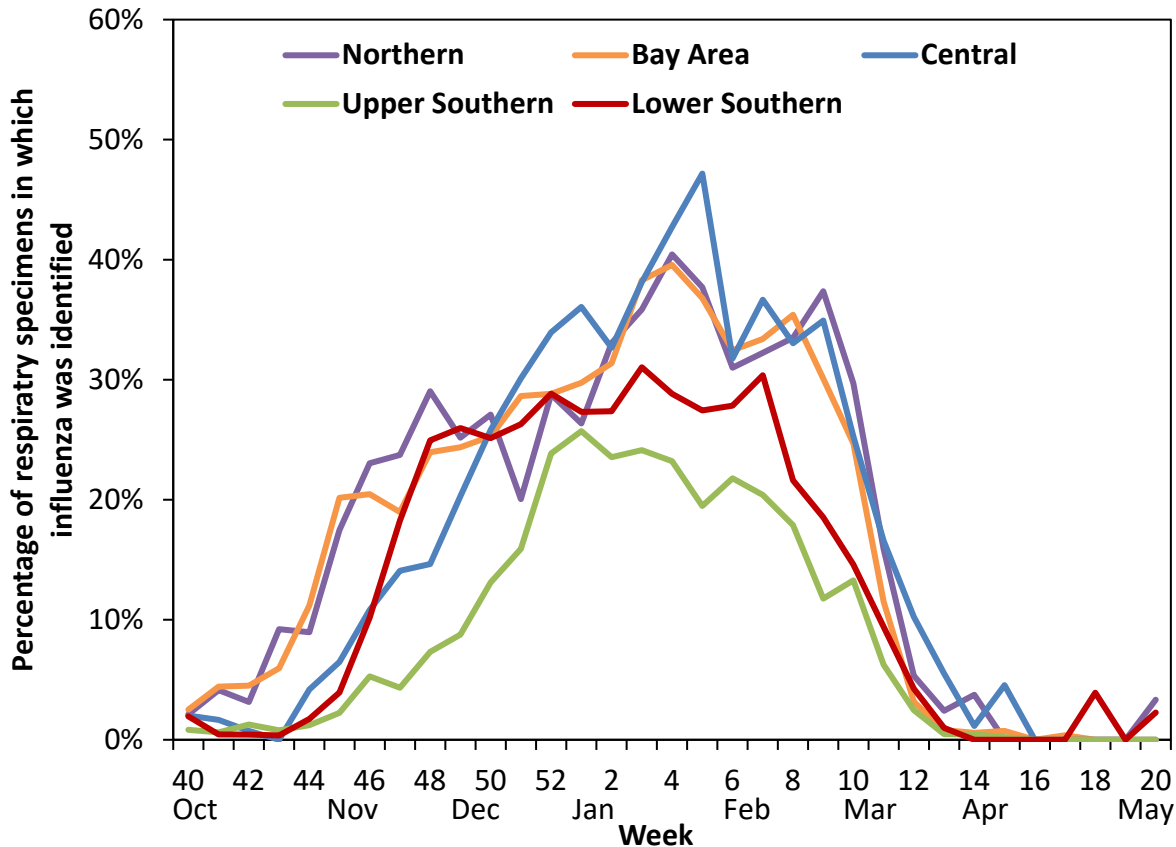


Figure 5. Percentage of specimens from which respiratory syncytial virus (RSV) was detected in clinical sentinel laboratories, 2015–2020

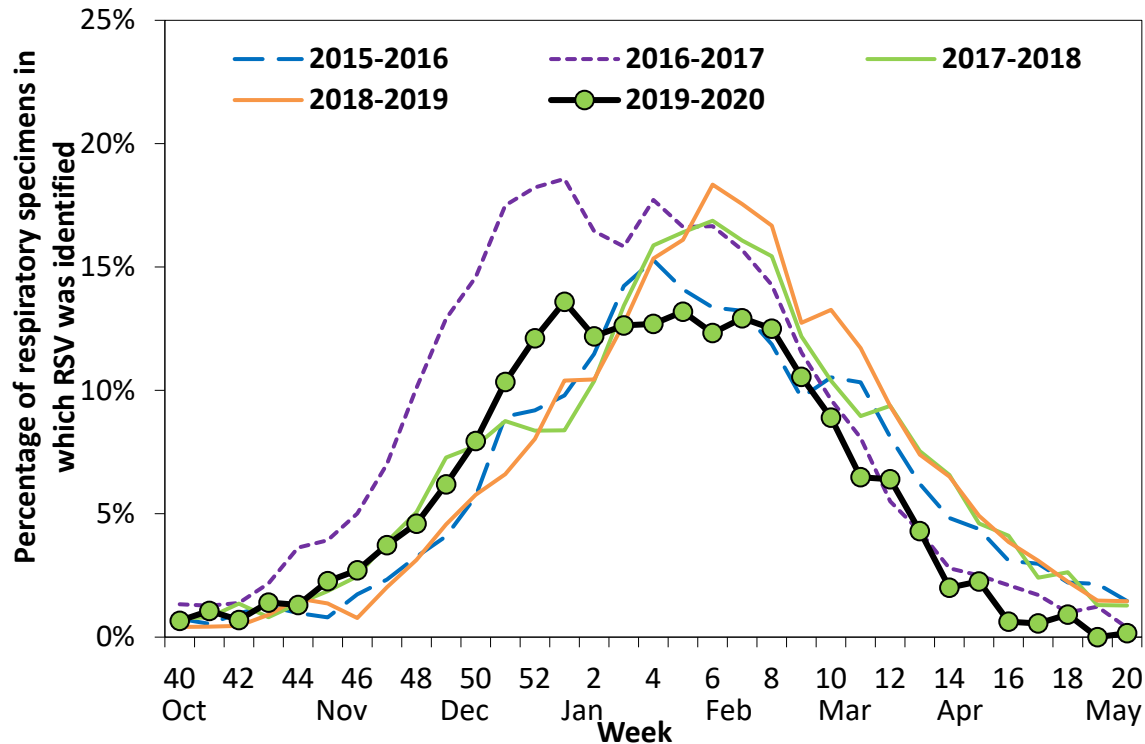
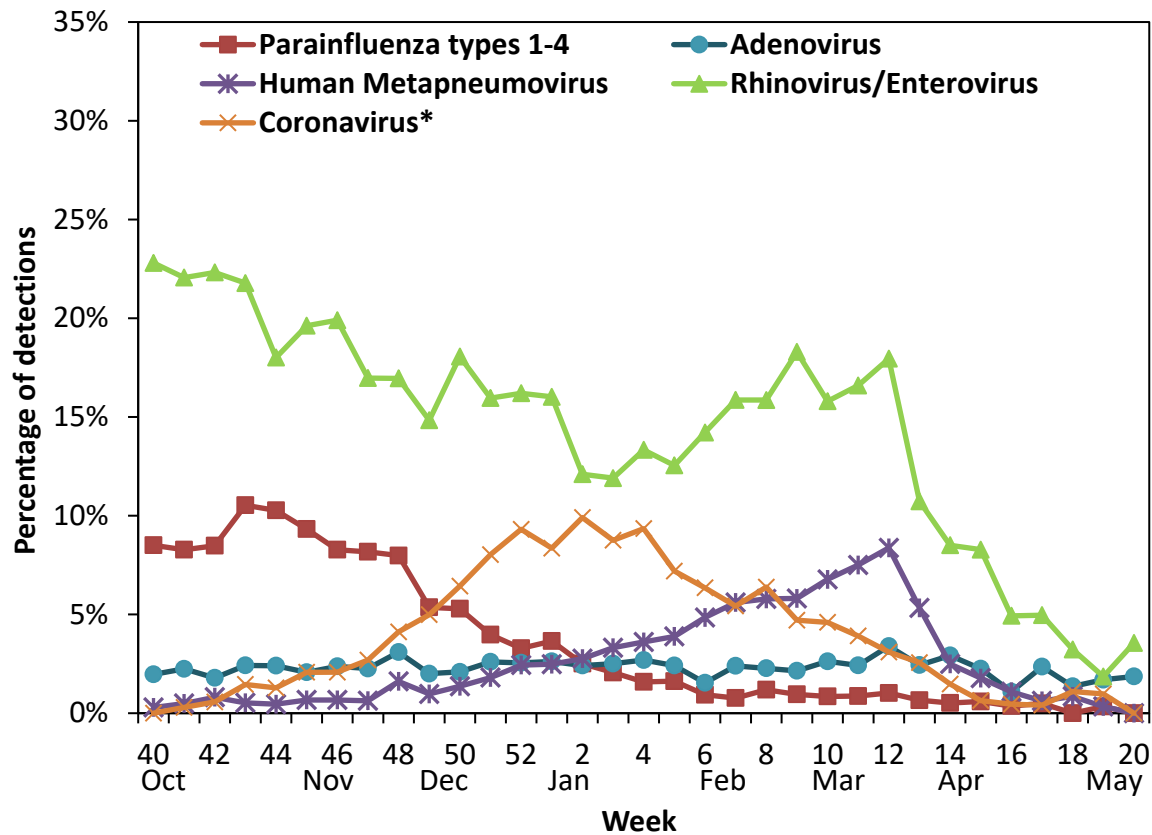


Figure 6. Percentage of specimens from which other respiratory viruses were detected in clinical sentinel laboratories, 2019–2020



*Coronaviruses identified include common human coronaviruses 229E, NL63, OC43, and HKU1. This figure does NOT include SARS-CoV-2.

3. Influenza Virus Characterization

Close monitoring of influenza viruses is required to better assess the potential impact on public health. CDC characterizes influenza viruses through one or more tests including [genomic sequencing](#), [hemagglutination inhibition \(HI\)](#) and/or neutralization based focus reduction assays (FRA). These data are used to compare how similar, or well-inhibited, currently circulating influenza viruses are to the reference viruses used for developing new influenza vaccines and to monitor evolutionary changes that continually occur in influenza viruses circulating in humans. Antigenic and genetic characterization of circulating influenza viruses gives an indication of the influenza vaccine's ability to induce an immune response against the wide array of influenza viruses that are co-circulating every season. However, annual [vaccine effectiveness estimates](#) are needed to determine how much protection was provided to the population by vaccination.

For nearly all influenza-positive surveillance samples received at CDC, genomic sequencing is performed to determine the genetic identity of circulating influenza viruses and to monitor the evolutionary trajectory of viruses circulating in our population. Virus gene segments are classified into genetic clades/subclades based on phylogenetic analysis. However, genetic changes that classify the clades/subclades do not always result in antigenic changes. Antigenic drift is a term used to describe gradual antigenic variation that occurs as viruses evolve changes to escape host immune pressure. Antigenic drift is evaluated by comparing antigenic properties of cell-propagated reference viruses representing currently recommended vaccine components with those of cell-propagated circulating viruses.

Influenza virus reference strains included in the 2019–2020 northern hemisphere influenza vaccine were:

- A/Kansas/14/2017 (H3N2)-like, which is a member of the 3c.3a clade
- A/Brisbane/02/2018 (H1N1pdm09)-like, which is a member of the 6B.1A clade
- B/Colorado/06/2017-like (Victoria lineage), which is a member of the V1A1.1 clade
- B/Phuket/3073/2013-like (Yamagata lineage), which is a member of the Y3 clade (only included in quadrivalent influenza vaccines)

The CDPH-VRDL and the Centers for Disease Control and Prevention (CDC) performed genomic sequencing on a total of 225 influenza positive samples collected throughout California during the 2019–2020 influenza season, of which 95 were antigenically characterized. The California genomic sequencing data and antigenic characterization data presented in this report represent specimens collected during September 30, 2019–March 16, 2020.

Thirty-eight influenza A (H3N2) viruses from California were genomically sequenced during the 2019–2020 influenza season, of which 14 were antigenically characterized. The 38 influenza A (H3N2) viruses were members of two clades/subclades, 3c.2a1b (34; 89.5%) and 3c.3a (4; 10.5%). Of the 14 influenza A (H3N2) viruses antigenically characterized, four (28.6%) were well-inhibited by A/Kansas/14/2017 (H3N2)-like antisera and 10 (71.4%) were poorly inhibited by A/Kansas/14/2017 (H3N2)-like antisera. All 10 of the poorly inhibited viruses were members of the 3c.2a1b subclade (Table 3a).

Ninety-four influenza A (H1N1)pdm09 viruses from California were genomically sequenced during the 2019–2020 influenza season, of which 43 were antigenically characterized. The 94 influenza A (H1N1)pdm09 viruses were members of a single clade/subclade, 6B.1A (94; 100%). Of the 43 influenza A (H1N1)pdm09 viruses antigenically characterized, 37 (86.0%) were well-inhibited by A/Brisbane/02/2018 (H1N1pdm09)-like antisera and 6 (14.0%) were poorly inhibited by A/Brisbane/02/2018 (H1N1pdm09)-like antisera (Table 3b).

Eighty-two influenza B (Victoria) viruses from California were genomically sequenced during the 2019–2020 influenza season, of which 29 were antigenically characterized. The 82 influenza B (Victoria) viruses were members of two clades/subclades, V1A.1 (6; 7.3%) and V1A.3 (76; 92.7%). Of the 29 influenza B (Victoria) viruses antigenically characterized, 15 (51.7%) were well-inhibited by B/Colorado/06/2017-like (Victoria lineage) antisera and 14 (48.3%) were poorly inhibited by B/Colorado/06/2017-like (Victoria lineage) antisera. All 14 of the poorly inhibited viruses were members of the V1A.3 clade/subclade (Table 3c).

Eleven influenza B (Yamagata) viruses from California were genomically sequenced during the 2019–2020 influenza season, of which nine were antigenically characterized. The 11 influenza B (Yamagata) viruses were members of a single clade/subclade, Y3 (11; 100%). All nine of influenza B (Yamagata) viruses that were antigenically characterized were well-inhibited by B/Phuket/3073/2013-like (Yamagata lineage) antisera (Table 3d).

Table 3 a–d. Influenza virus antigenic characterization and genomic sequencing by influenza A subtype and influenza B lineage type — California, 2019–2020 influenza season

a. Antigenic characterization of influenza A (H3N2) viruses by virus clade/subclade

Antigenic Characterization	Virus Clade/ Subclade 3C.2a1b	Virus Clade/ Subclade 3C.3a [*]	Total
Well inhibited by A/Kansas/14/2017*	3	1	4
Poorly inhibited by A/Kansas/14/2017*	10	0	10
Not antigenically characterized	21	3	24
Total A (H3N2)	34	4	38

b. Antigenic characterization of influenza A (H1N1)pdm09 viruses by virus clade/subclade

Antigenic Characterization	Virus Clade/ Subclade 6B.1	Virus Clade/ Subclade 6B.1A [†]	Total
Well inhibited by A/Brisbane/02/2018*	0	37	37
Poorly inhibited by A/Brisbane/02/2018*	0	6	6
Not antigenically characterized	0	51	51
Total A (H1N1)pdm09	0	94	94

* A/Kansas/14/2017 is the influenza A (H3N2) component included in the 2019–2020 quadrivalent and trivalent influenza vaccines and is a member of the 3c.3a clade

† A/Brisbane/02/2018 is the influenza A (H1N1)pdm09 component included in the 2019–2020 quadrivalent and trivalent influenza vaccines and is a member of the 6B.1A clade

c. Antigenic characterization of influenza B (Victoria) viruses by virus clade/subclade

Antigenic Characterization	Virus Clade/ Subclade V1A.1*	Virus Clade/ Subclade V1A.3	Total
Well inhibited by B/Colorado/06/2017*	3	12	15
Poorly inhibited by B/Colorado/06/2017*	0	14	14
Not antigenically characterized	3	50	53
Total B (Victoria)	6	76	82

d. Antigenic characterization of influenza B (Yamagata) viruses by virus clade/subclade

Antigenic Characterization	Virus Clade/ Subclade Y3[†]	Total
Well inhibited by B/Phuket/3073/2013*	9	9
Poorly inhibited by B/Phuket/3073/2013*	0	0
Not antigenically characterized	2	2
Total B (Yamagata)	11	11

4. Antiviral Resistance Testing

The CDPH-VRDL monitors antiviral resistance (AVR) for a select subset of influenza A and B positive specimens using two molecular methods: 1) a high throughput pyrosequencing assay to detect mutations known to confer neuraminidase inhibitor (NAI) resistance; and 2) next generation sequencing. Of the 287 influenza specimens tested by the CDPH-VRDL during the 2019–2020 influenza season, none were found to be resistant to NAIs (Table 4).

Table 4. Number of specimens tested for resistance to neuraminidase inhibitors by molecular testing method, California, 2019–2020 season[‡]

	Neuraminidase Inhibitor Resistance Detected by Pyrosequencing	Neuraminidase Inhibitor Resistance Detected by Next Generation Sequencing
Influenza A (H1N1)pdm09	0/27	0/94
Influenza A (H3N2)	0/1	0/38
Influenza B	0/34	0/93

* B/Colorado/06/2017-like is the influenza B (Victoria) lineage component included in the 2019–2020 quadrivalent and trivalent influenza vaccines and is a member of the V1A.1 clade

[†] B/Phuket/3073/2013 is the influenza B (Yamagata) component included in the 2019–2020 quadrivalent influenza vaccine and is a member of the Y3 clade

[‡] California data are from specimens collected during September 30, 2019–March 16, 2020

CDC also performs antiviral resistance testing as part of its routine national surveillance. As of the last report published by CDC containing antiviral resistance testing information, which contained data through the week ending April 4, 2020, CDC reported testing 2,433 influenza viruses during September 29, 2019 through April 4, 2020 from throughout the United States, including California, for resistance to the influenza neuraminidase inhibitor antiviral medications recommended for use against seasonal influenza (oseltamivir, peramivir, and zanamivir) using next generation sequencing. In addition, 2,541 influenza viruses were tested for resistance to baloxavir, a PA endonuclease inhibitor, using next generation sequencing. All 502 influenza A (H3N2) viruses tested for oseltamivir, peramivir, and zanamivir susceptibility were susceptible to all three medications. No viruses with reduced susceptibility to baloxavir were detected among 584 influenza A (H3N2) viruses tested. Among 885 influenza A (H1N1)pdm09 viruses tested for oseltamivir, peramivir, and zanamivir susceptibility, four (0.5%) showed highly reduced susceptibility to oseltamivir and peramivir and none showed reduced susceptibility to zanamivir. Among 884 influenza A (H1N1)pdm09 viruses tested for baloxavir susceptibility, no viruses were found to have reduced susceptibility. Among 954 influenza B (Victoria) viruses tested for oseltamivir, peramivir, and zanamivir susceptibility, one (0.1%) showed reduced susceptibility to oseltamivir, one (0.1%) showed highly reduced susceptibility to peramivir, and 2 (0.2%) showed reduced susceptibility to zanamivir. Among 978 influenza B (Victoria) viruses also tested for baloxavir susceptibility, no resistant viruses were detected. Among 92 influenza B (Yamagata) viruses tested, all were found to be susceptible to oseltamivir, peramivir, and zanamivir. Among 95 influenza B (Yamagata) viruses also tested for baloxavir susceptibility, no resistant viruses were detected.⁴

A total of 556 additional viruses (211 A(H1N1)pdm09, 32 A(H3N2), and 313 B) were analyzed for resistance to neuraminidase inhibitors by pyrosequencing assay. Three (1.4%) of the 211 A(H1N1)pdm09 viruses tested had the H275Y amino acid substitution in the neuraminidase and showed highly reduced susceptibility to oseltamivir and peramivir. No molecular markers associated with reduced or highly reduced inhibition by neuraminidase inhibitors were detected in A(H3N2) and type B viruses tested.⁴

5. Novel Influenza A Viruses

No novel influenza viruses were detected in California by the CDPH-VRDL or RLN laboratories by real-time reverse transcription polymerase chain reaction (rRT-PCR) during the 2019–2020 season.

B. Case-Based Surveillance

1. Influenza-associated Pediatric Deaths

Laboratory-confirmed influenza-associated pediatric deaths (<18 years of age) are nationally notifiable and are also reportable in California [Title 17, California Code of Regulations (CCR) §2500].

During the 2019–2020 influenza season, CDPH received 22 reports of influenza-associated pediatric deaths. Seventeen (77%) had onset during the weeks ending December 21, 2019 through February 29, 2020, during which more than 20% of specimens tested positive for influenza based on data from clinical sentinel laboratories, and five (23%) had onset outside of

this period. Of the 22 influenza-associated pediatric deaths, 15 (68%) had at least one underlying medical condition, including those conditions defined by the Advisory Committee for Immunization Practices (ACIP) as being associated with severe influenza⁵, and seven (32%) were previously healthy. Eight (36%) of the 22 influenza-associated pediatric deaths, died outside of the hospital, in the emergency department, or within 24 hours of hospital admission. Eleven (50%) were not vaccinated against influenza during the 2019–2020 influenza season, five (23%) were vaccinated, and six (27%) had unknown vaccination status. Of the 22 influenza-associated deaths, 10 (45%) were due to influenza A (eight [80%] were influenza A (H3N2), one [10%] was influenza A (H1N1)pdm09, and one [10%] was influenza A with unknown subtype) and 12 (55%) were due to influenza B (six [50%] were influenza B (Victoria) and six [50%] were influenza B with unknown lineage type).

2. California Emerging Infections Program Data: Influenza-associated Hospitalizations

The California Emerging Infections Program (CEIP), Influenza Surveillance Network (FluSurv-NET) conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations among persons of all ages in Alameda, Contra Costa, and San Francisco counties. FluSurv-NET is a national network which covers over 70 counties in the 10 Emerging Infections Program (EIP) states (CA, CO, CT, GA, MD, MN, NM, NY, OR, and TN) and three additional states (MI, OH, and UT).

During the 2019–2020 season, the incidence of influenza-associated hospitalizations per 100,000 population began increasing in December and peaked during the week ending January 25, 2020 with an incidence of 5.0 influenza hospitalizations per 100,000 population (Figure 7). While the peak rate was substantially lower than the peak rate during the 2017–2018 influenza season (20.4 influenza hospitalizations per 100,000), it was comparable to the peak rate during the 2018–2019 influenza season (5.6 influenza hospitalizations per 100,000). Of the 2,127 patients hospitalized in the three counties monitored by CEIP for influenza 1,714 (80.6%) had influenza A infections, 404 (19.0%) had influenza B infections, and 9 (0.4%) had influenza A and B co-infections. The highest cumulative rate of hospitalization was among adults aged >64 years, followed by the 50–64 years and 0–4 years age groups (Figure 8). Patients >64 years of age accounted for 47.5% of the total reported hospitalized cases.

Figure 7. Incidence of influenza-associated hospitalizations per 100,000 population in CEIP counties, 2017–2020

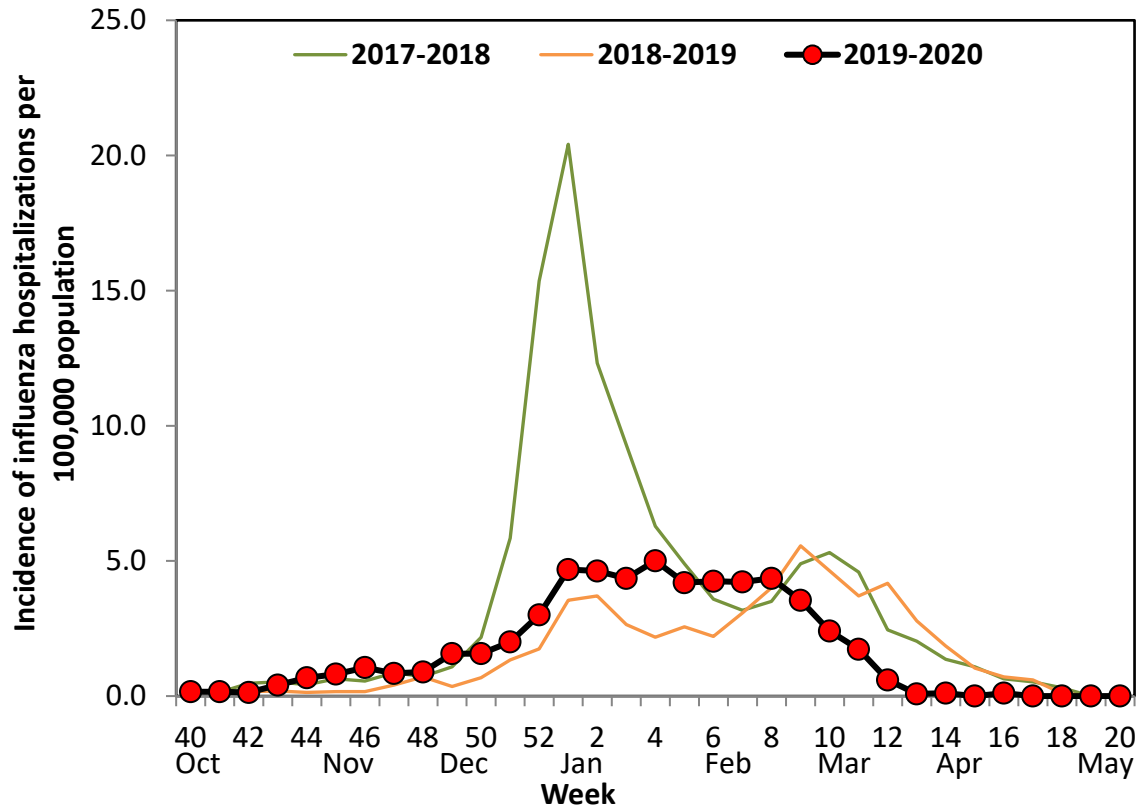
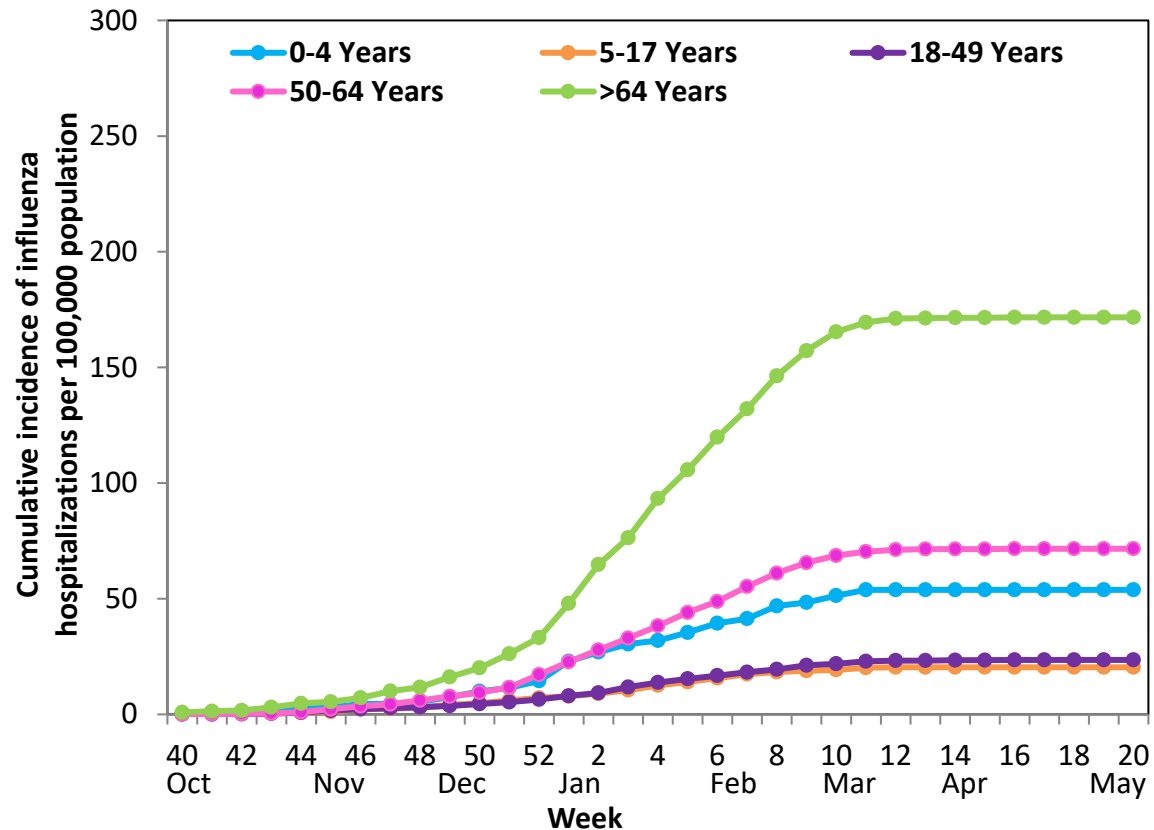


Figure 8. Cumulative incidence of influenza hospitalizations per 100,000 population in CEIP counties by age group, 2019–2020



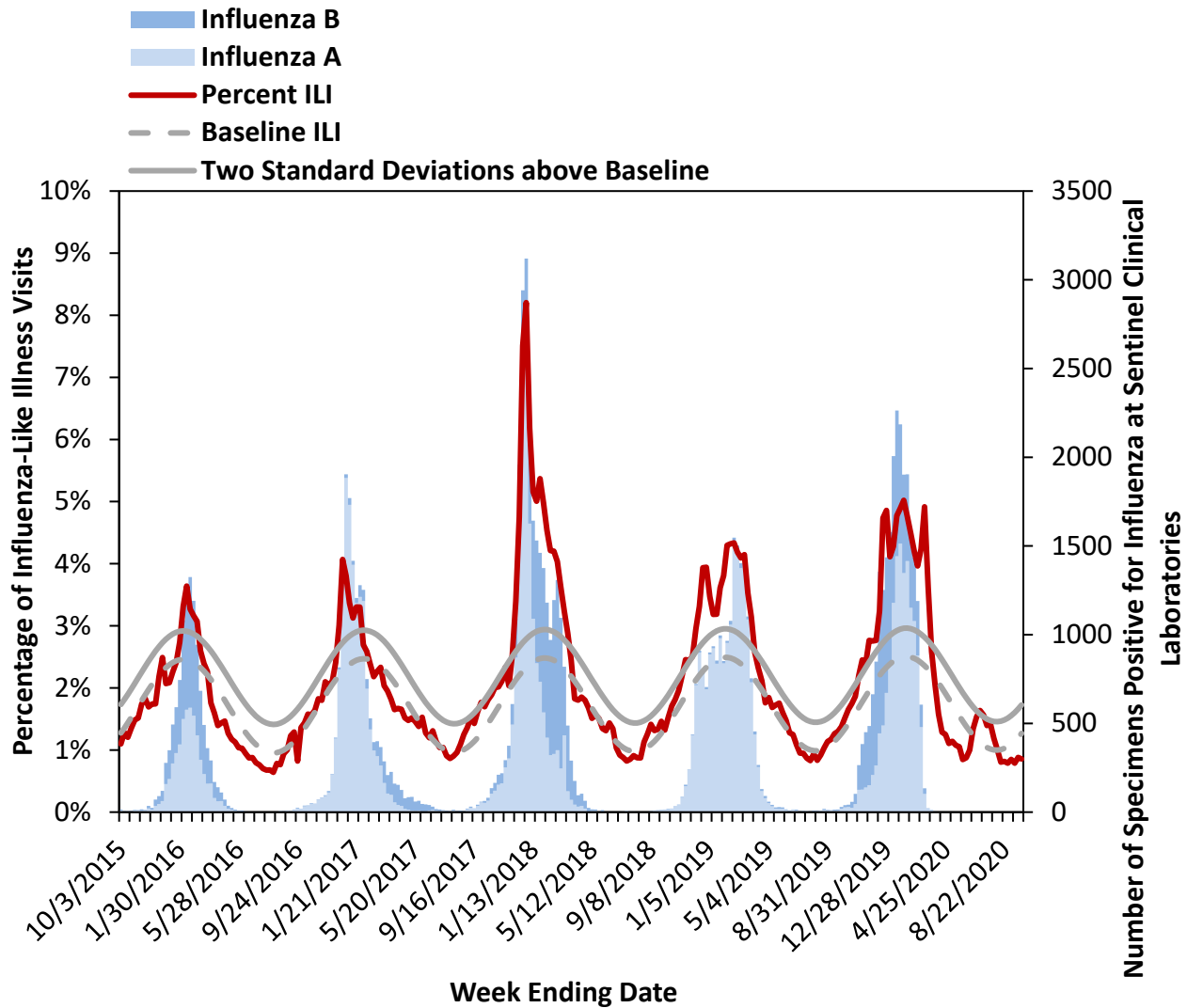
C. Syndromic Surveillance

1. Influenza-like Illness Outpatient Surveillance (Sentinel Providers)

In collaboration with CDC, the CDPH works with volunteer sentinel providers throughout the state to conduct year-round surveillance for ILI in outpatients. Sentinel providers may be individual practitioners or may represent whole healthcare systems in a variety of outpatient settings including, but not limited to, hospital outpatient clinics, emergency departments, and student health services. Sentinel providers report on a weekly basis the number of patients with ILI and the total number of patients seen for any reason. ILI is defined as any illness with (1) fever ($\geq 100^{\circ}\text{F}$ or 37.8°C) and (2) cough and/or sore throat, in the absence of a known cause other than influenza.

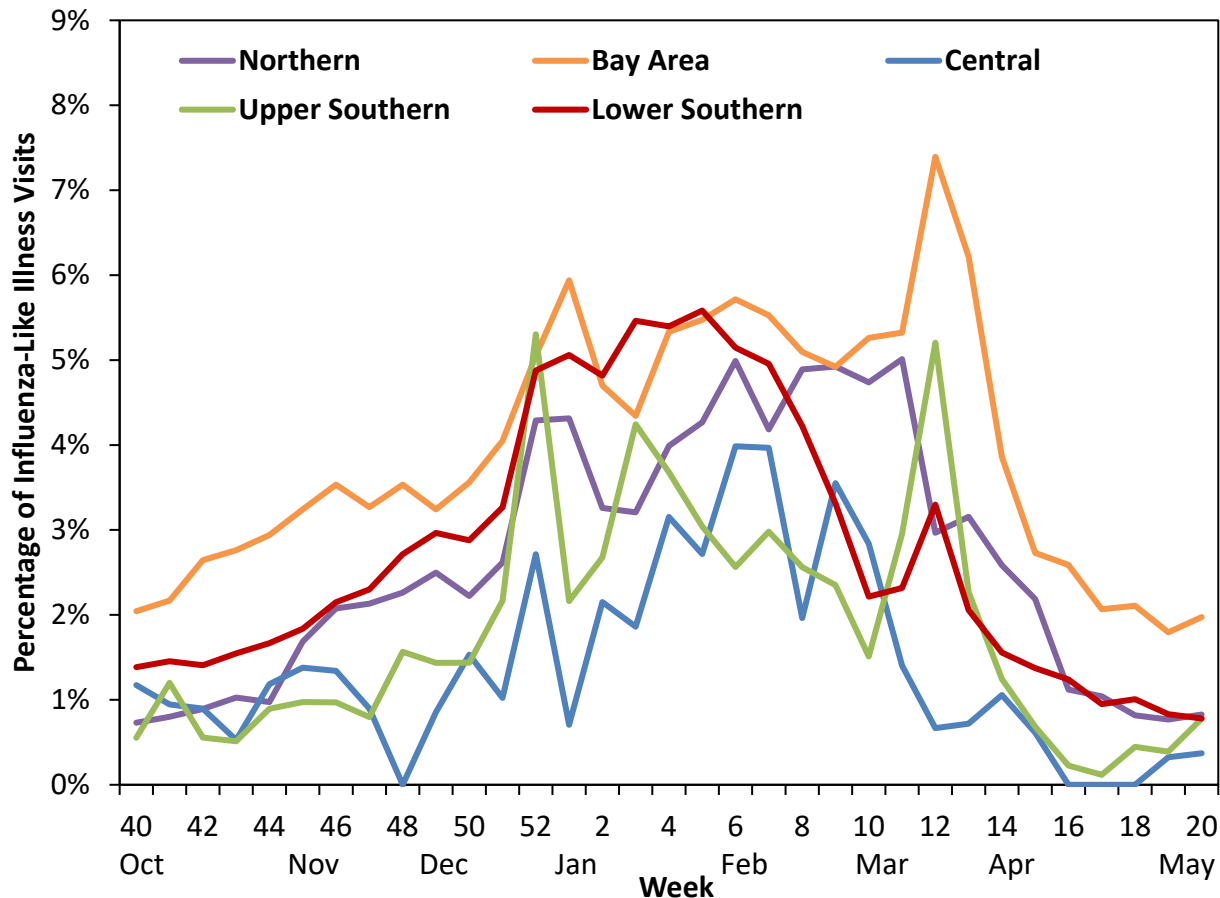
In California, 121 sentinel providers reported ILI activity on a regular basis (i.e., at least 17 of the 33 weeks from September 29, 2019 to May 16, 2020). There was minimal ILI activity until early November, when sentinel providers began reporting increases in patients with ILI (Figure 9). The percentage of ILI visits among outpatients had three peaks in activity. The first peak occurred during the week ending January 4, 2020 (4.9%), corresponding to a period when influenza B (Victoria) activity was near its peak and influenza A (H1N1)pdm09 activity was increasing, and the second peak occurred during the week ending February 8, 2020 (5.0%), corresponding to the period when influenza A (H1N1)pdm09 activity was peaking and influenza B (Victoria) activity was still elevated. The third peak occurred during the week ending March 21, 2020 (4.9%), corresponding to a period of sharp decline in influenza activity, but coinciding with increases in awareness and community transmission of SARS-CoV-2, the virus that cause COVID-19, which might have changed health-care seeking behaviors of person experiencing ILI. ILI activity declined sharply as shelter-in-place orders to stop the transmission of SARS-CoV-2 were enacted in California on March 16, 2020.^{3,6} The percentage of visits for ILI exceeded two standard deviations above baseline levels between the weeks ending November 9, 2019 and March 28, 2020. Most California regions also experienced more than one peak in outpatient ILI activity as well; however, the number, magnitude, and timing of the peaks varied by region (Figure 10).

Figure 9. Percentage of influenza-like illness visits among patients seen by California Sentinel Providers, 2015–2020*



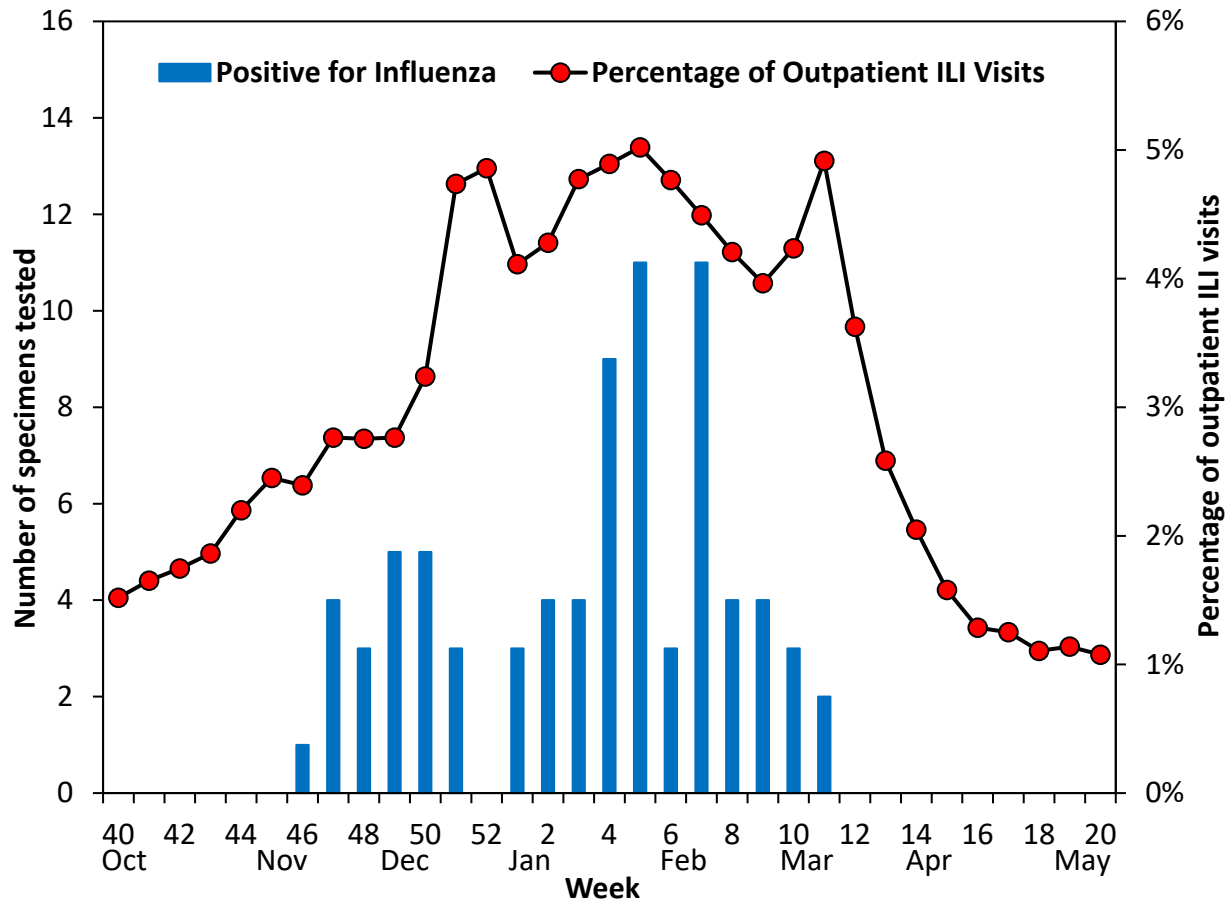
* The seasonal baseline was calculated using a regression model applied to data from the previous five years. Two standard deviations above the seasonal baseline is the point at which the observed percentage of ILI is significantly higher than would be expected at that time of the year.

Figure 10. Percentage of influenza-like illness visits among patients seen by California Sentinel Providers by California region, 2019–2020



Sentinel providers voluntarily submit specimens from patients with ILI to the CDPH-VRDL for influenza testing. Many of these specimens are sent to CDC for further characterization, providing important information about what influenza virus strains are circulating in the community. From September 29, 2019 through May 16, 2020, sentinel providers submitted 143 respiratory specimens; 79 (55.2%) were positive for influenza. Of these, 39 (49.4%) were influenza A and 40 (50.6%) were influenza B. Of the 39 positive influenza A specimens, one (2.6%) was A (H3N2), 34 (87.2%) were A (H1N1)pdm09, and four (10.3%) were not subtyped. Of the 40 positive influenza B specimens, none (0.0%) were B (Yamagata), 39 (97.5%) were B (Victoria), and one (2.5%) was not lineage-typed. The number of specimens submitted by sentinel providers that tested positive for influenza peaked during the weeks ending February 1, 2020 and February 15, 2020, which coincided with the second peak in ILI activity (Figure 11). The first peak in ILI activity during the week ending December 28, 2019 coincided with a drop in submitted specimens, which was likely due to the Christmas and New Year's holidays.

Figure 11. Sentinel Provider specimens testing positive by week of specimen collection and percentage of influenza-like illness visits by week of visit, September 29, 2019–May 16, 2020



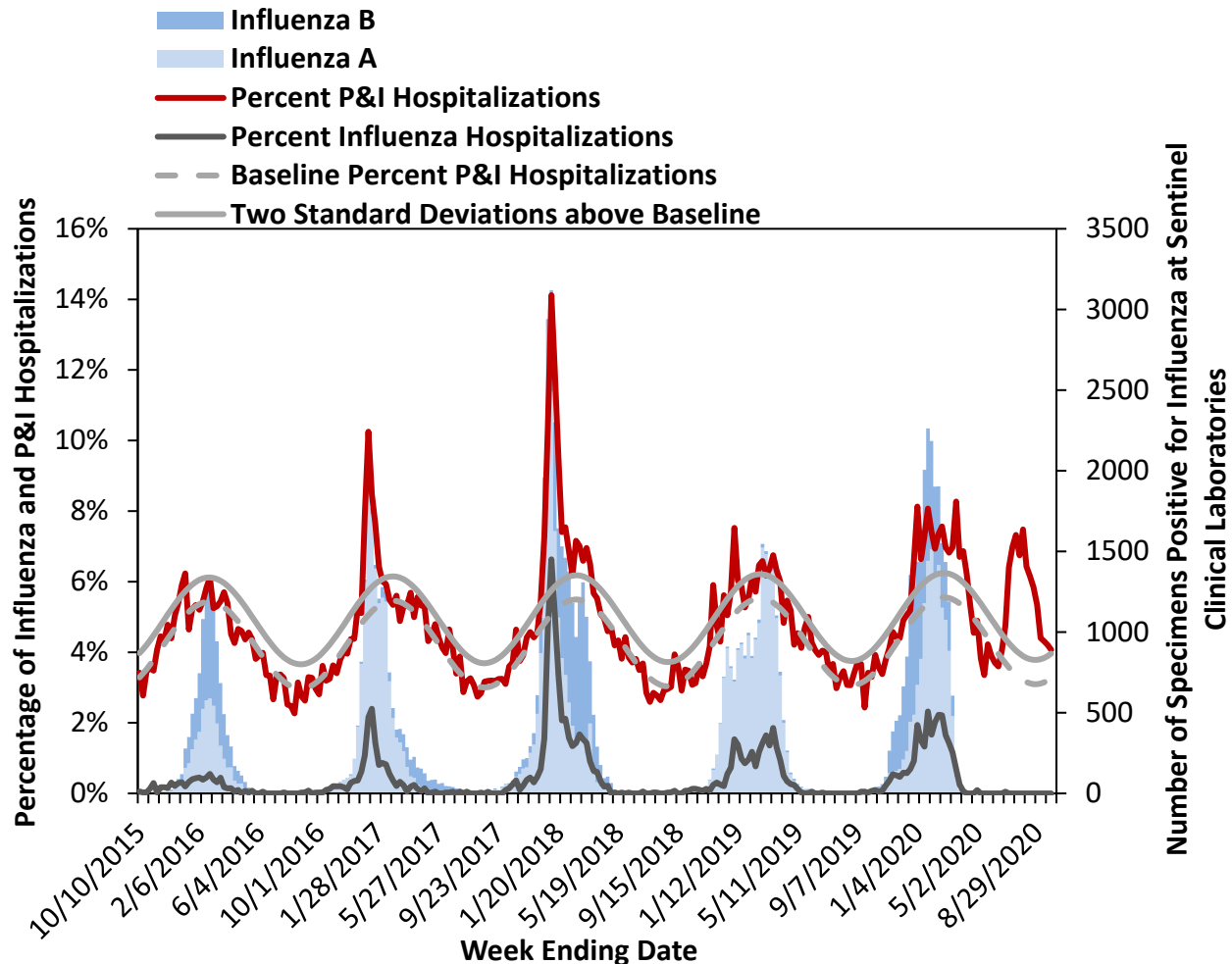
2. Kaiser Permanente Northern California Pneumonia and Influenza Admission Data

The CDPH collaborates with Northern California Kaiser Permanente to monitor trends in pneumonia and influenza-associated hospitalizations. Patients with admission diagnoses of “flu,” “pneumonia,” or “influenza” are defined as pneumonia and influenza (P&I) admissions. The number of P&I admissions is divided by the total number of hospital admissions occurring in the same time period to estimate the percentage of P&I admissions. Admissions for pregnancy, labor and delivery, birth, and outpatient procedures are excluded from the denominator. Please note that pneumonia and influenza admissions serve as a proxy for influenza activity but do not necessarily represent laboratory-confirmed influenza infections. During the 2019–2020 influenza season, pneumonia and influenza admissions data also reflect SARS-CoV-2 activity beginning in March.

During the 2019–2020 influenza season, the percentage of P&I admissions at Northern California Kaiser Permanente hospitals began gradually increasing in November, exceeding two standard deviations above baseline levels the week ending December 28, 2019, and fluctuated between 6.2% and 8.3% during the weeks ending December 28, 2019 and April 11, 2020 without a clear peak week. The percentage of P&I admissions decreased to baseline levels in mid-April; however, a second period of elevated activity occurred during late June through the end of the surveillance period in September, peaking at 7.5% during the week ending August 1, 2020. In contrast, the

percentage of admissions at Northern Kaiser Permanente Hospitals for influenza, excluding admissions for pneumonia where influenza was not mentioned, began gradually increasing in November, peaking at 2.3% during the week ending January 25, 2020, and declined to at or near 0% by the week ending April 4, 2020. The percentage of hospital admissions for influenza closely aligns with the number of influenza positive specimens identified at clinical sentinel laboratories, while the percentage of admissions for pneumonia and influenza was more likely to be impacted by the emergence and continued circulation of SARS-CoV-2 in the spring and summer of 2020 (Figure 12).

Figure 12. Percentage of influenza and pneumonia & influenza (P&I) admissions in Northern California Kaiser Permanente hospitals, 2015–2020*



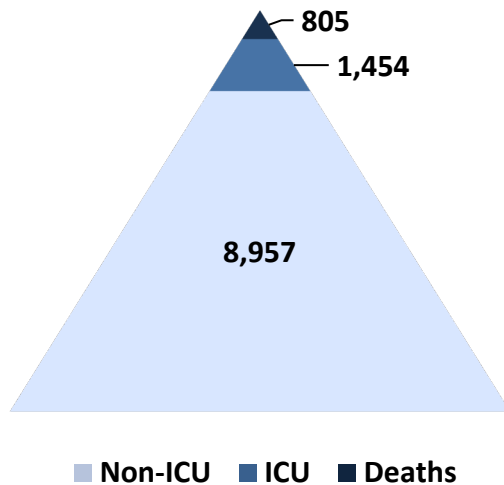
* The seasonal baseline was calculated using a regression model applied to data from the previous five years. Two standard deviations above the seasonal baseline is the point at which the observed percentage of pneumonia and influenza hospitalizations in Kaiser Permanente hospitals in Northern California is significantly higher than would be expected at that time of the year.

During September 29, 2019–September 26, 2020, the majority of hospitalizations due to pneumonia and influenza did not result in intensive care unit (ICU) admission or death; however, 1,454 ICU admissions and 805 deaths occurred among persons with P&I admission diagnoses (Figure 13a). Four thousand twenty-five (44.9%) of the P&I non-ICU hospital admissions, 702 (48.3%) of the P&I ICU admissions, and 443 (55.0%) of the P&I deaths were admitted after the

week ending March 14, 2020, when influenza activity sharply declined and SARS-CoV-2 activity was increasing.³ In contrast, only 30 (3.4%) of the 874 influenza non-ICU hospital admissions, five (3.1%) of the 161 influenza ICU admissions, and three (7.3%) of the 41 influenza deaths were admitted after the week ending March 14, 2020 (Figure 13b). The largest proportion of P&I admissions occurred among person ≥ 65 years of age across all severity categories, especially among deaths (Figure 14a). Similar patterns were seen among influenza admissions (Figure 14b).

Figure 13. Number of non-ICU admissions, ICU admissions, and deaths associated with (a) P&I and (b) influenza admissions in Kaiser Permanente Northern California hospitals, September 29, 2019–September 26, 2020

(a) Pneumonia and Influenza (P&I)



(b) Influenza

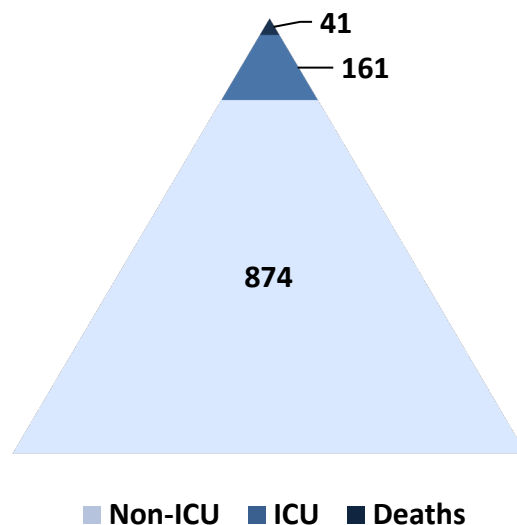
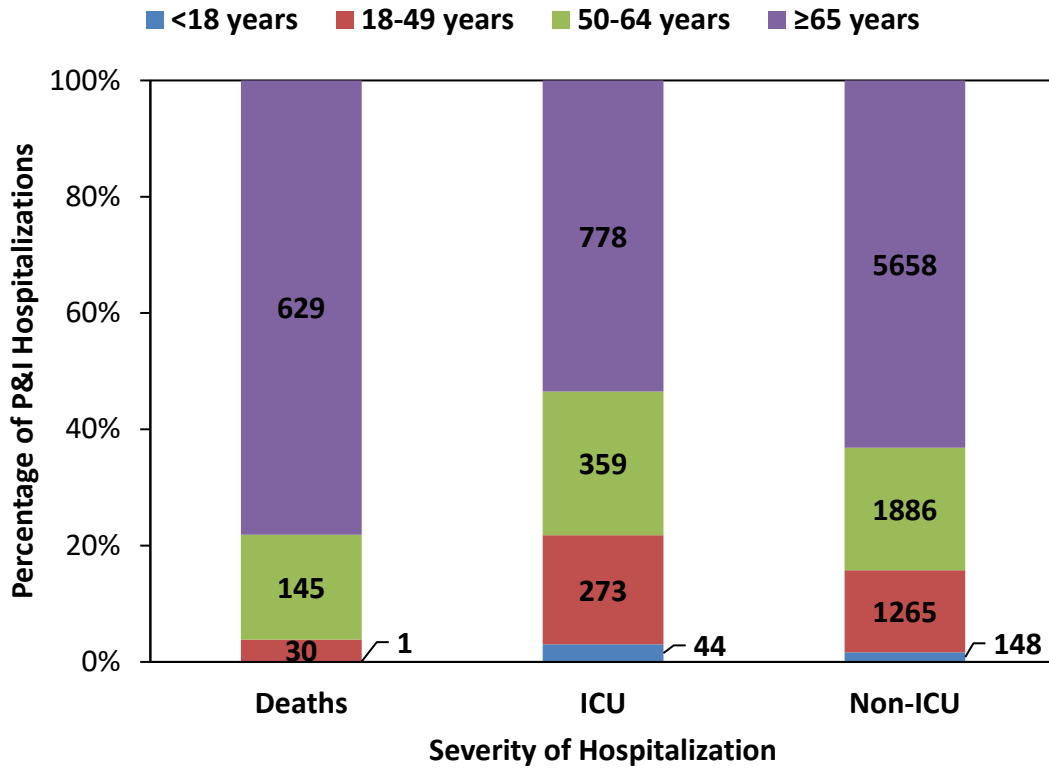
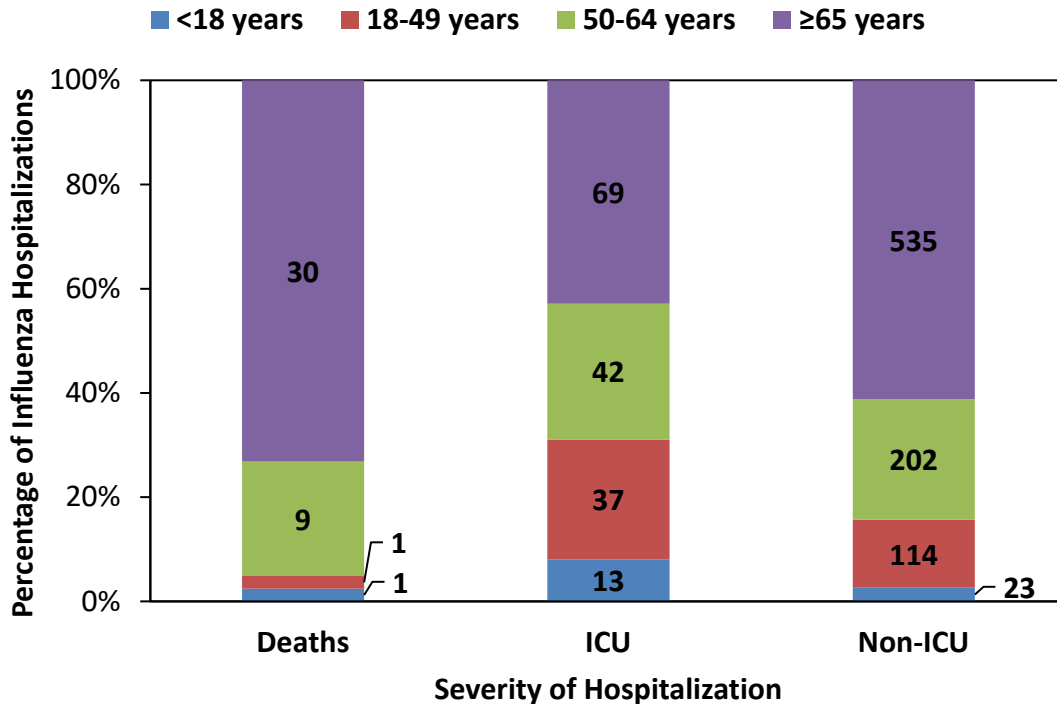


Figure 14. Age group distribution of non-ICU admissions, ICU admissions, and deaths associated with (a) P&I and (b) influenza admissions in Kaiser Permanente Northern California hospitals, September 29, 2019–September 26, 2020

(a) Pneumonia and Influenza (P&I)



(b) Influenza



3. Influenza Mortality Surveillance from Death Certificates

Deaths occurring in California among residents who had influenza noted in any cause of death field on the death certificate (influenza specified in a text cause of death field or an influenza ICD-10 code in a coded cause of death field) are defined as influenza-coded deaths. The percentage of influenza-coded deaths is calculated by dividing the number of influenza-coded deaths by the total number of all cause deaths during the same period. Influenza-coded deaths are not necessarily laboratory-confirmed and are an underestimate of all influenza-associated deaths.

During September 29, 2019–September 26, 2020, 889 influenza-coded deaths were identified (Figure 15). The percentage of influenza-coded deaths began increasing in December, had an early peak of 1.2% during the week ending January 25, 2020, and was followed by a brief period of decline before increasing again to a second, higher, peak of 1.4% during the week ending February 15, 2020 (Figure 16). The percentage of influenza-coded deaths remained elevated through early April. The number of influenza-coded deaths during the 2019–2020 influenza season was higher than what was seen during the 2015–2016, 2016–2017, and 2018–2019 influenza seasons, but was substantially lower than what was seen during the 2017–2018 influenza season (Table 5).

Figure 15. Number of influenza-coded deaths identified from death certificates by week of death, September 29, 2019–September 26, 2020

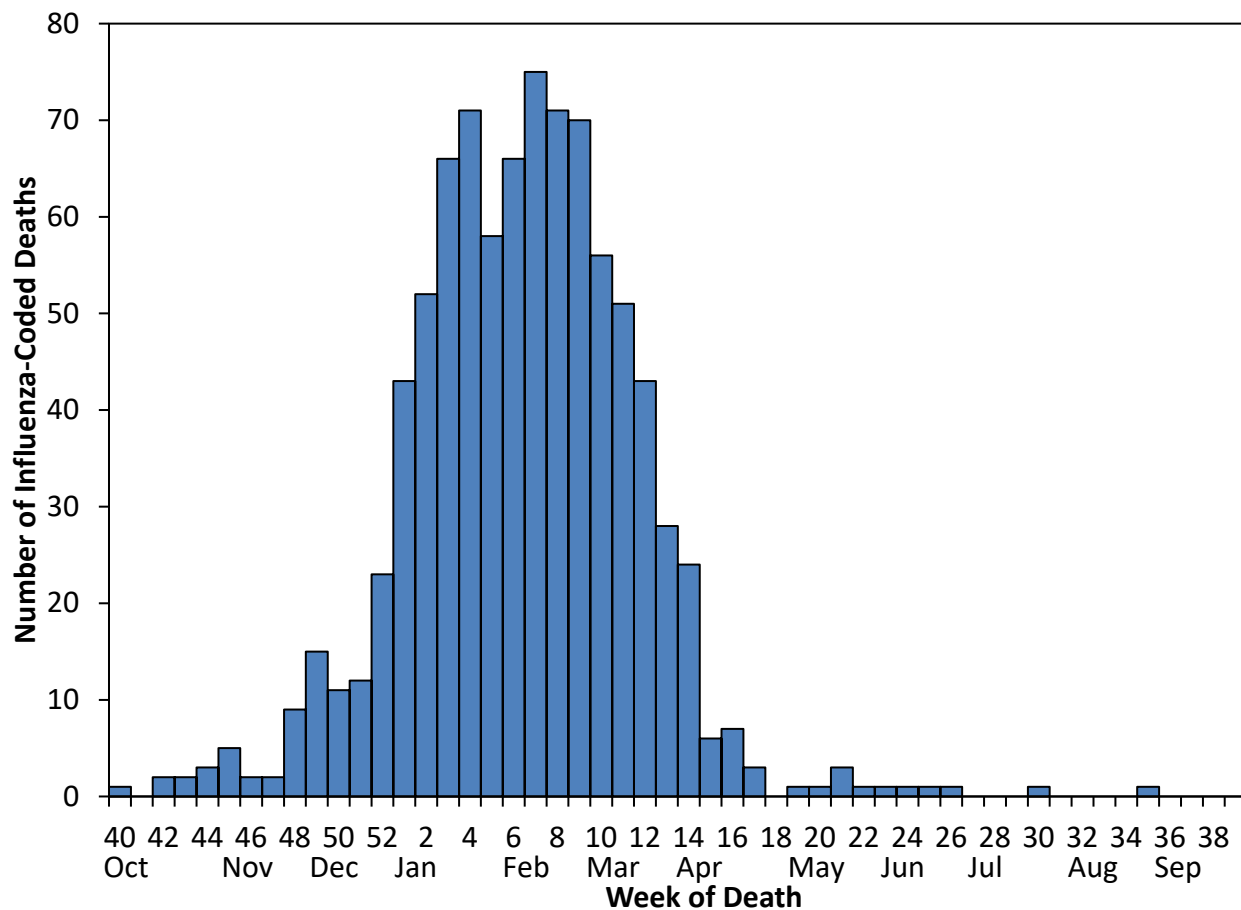


Figure 16. Percentage of influenza-coded deaths occurring in California among California residents, 2015–2020

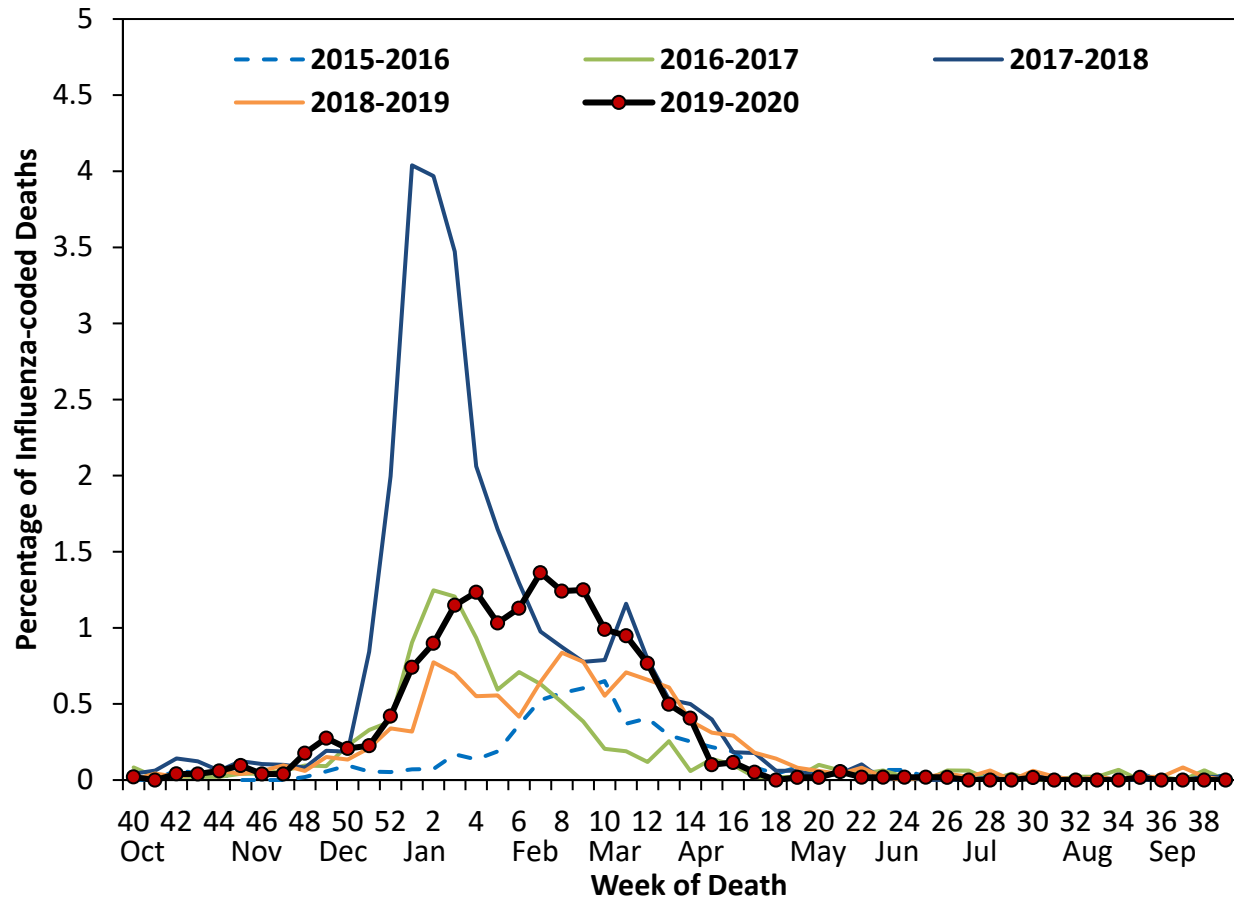


Table 5. Number and Percentage of Influenza-coded Deaths Occurring in California among California Residents, 2015–2016 through 2019–2020 Influenza Seasons

Influenza Season*	Total Number of Influenza-coded Deaths	Peak Percentage of Influenza-coded Deaths
2015–2016	326	0.7%
2016–2017	579	1.2%
2017–2018	1,666	4.0%
2018–2019	613	0.8%
2019–2020	889	1.4%

* 2015–2016 influenza season: October 4, 2015–October 1, 2016; mixed influenza A and influenza B season

2016–2017 influenza season: October 2, 2016–September 30, 2017; influenza A (H3N2) predominant season

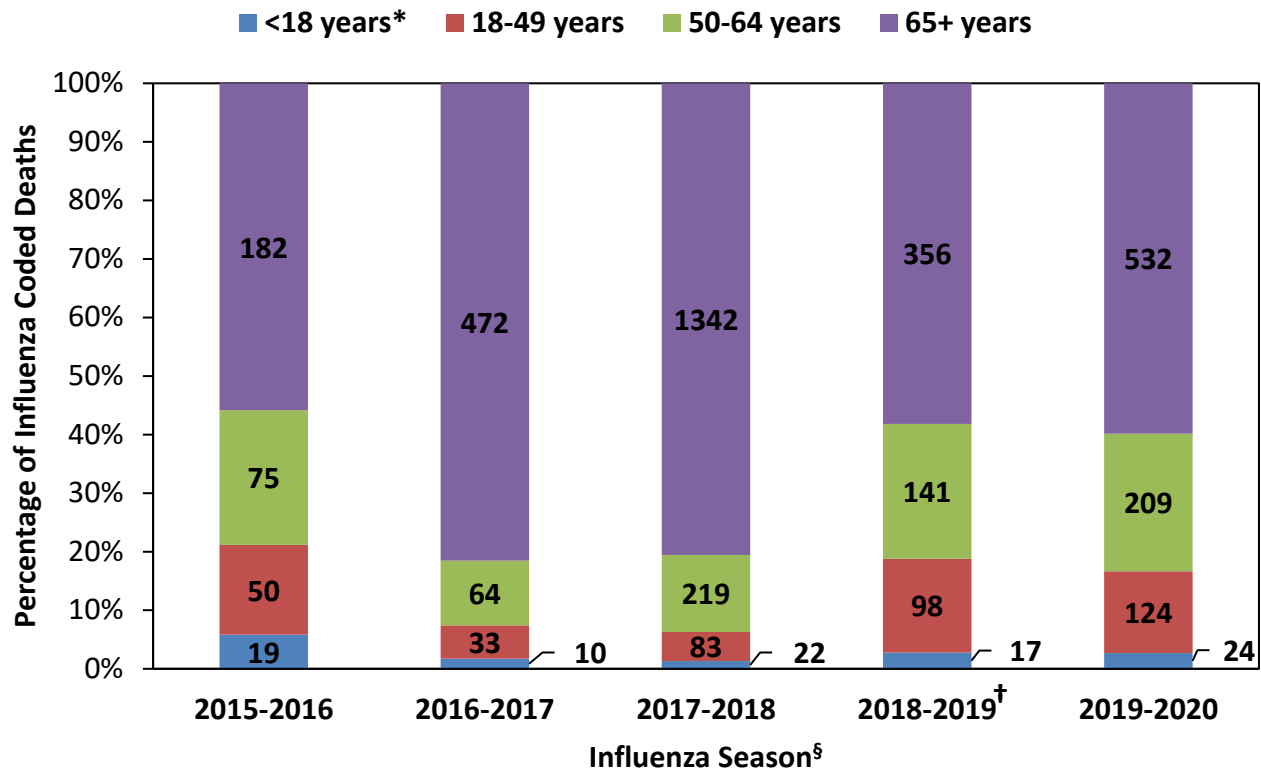
2017–2018 influenza season: October 1, 2017–September 29, 2018; influenza A (H3N2) predominant season

2018–2019 influenza season: September 30, 2018–September 28, 2019; mixed influenza A (H1N1)pdm09 and influenza A (H3N2) season

2019–2020 influenza season: September 29, 2019–September 26, 2020; mixed influenza B (Victoria) and influenza A (H1N1)pdm09 season

During the 2019–2020 influenza season, fewer deaths occurred among persons <65 years of age (40.2%) than among persons ≥65 years of age; however, the percentage of deaths occurring among persons <65 years of age is consistent with other seasons during which influenza A (H1N1)pdm09 has circulated in greater numbers, such as the 2015–2016 and 2018–2019 seasons (Figure 17).

Figure 17. Age distribution of influenza-coded deaths occurring in California among California residents, 2015–2016 through 2019–2020 seasons



* Methods used to identify pediatric influenza-coded deaths on death certificates differ from those used to identify the influenza-associated pediatric deaths presented on page 14. Please see pages 14 and 24 for additional details.

[†] One death during the 2018–2019 influenza season has unknown age and is not included in the figure.

[§] 2015–2016 influenza season: October 4, 2015–October 1, 2016; mixed influenza A and influenza B season

2016–2017 influenza season: October 2, 2016–September 30, 2017; influenza A (H3N2) predominant season

2017–2018 influenza season: October 1, 2017–September 29, 2018; influenza A (H3N2) predominant season

2018–2019 influenza season: September 30, 2018–September 28, 2019; mixed influenza A (H1N1)pdm09 and influenza A (H3N2) season

2019–2020 influenza season: September 29, 2019–September 26, 2020; mixed influenza B (Victoria) and influenza A (H1N1)pdm09 season

D. Outbreaks of Respiratory Illness, Including Influenza

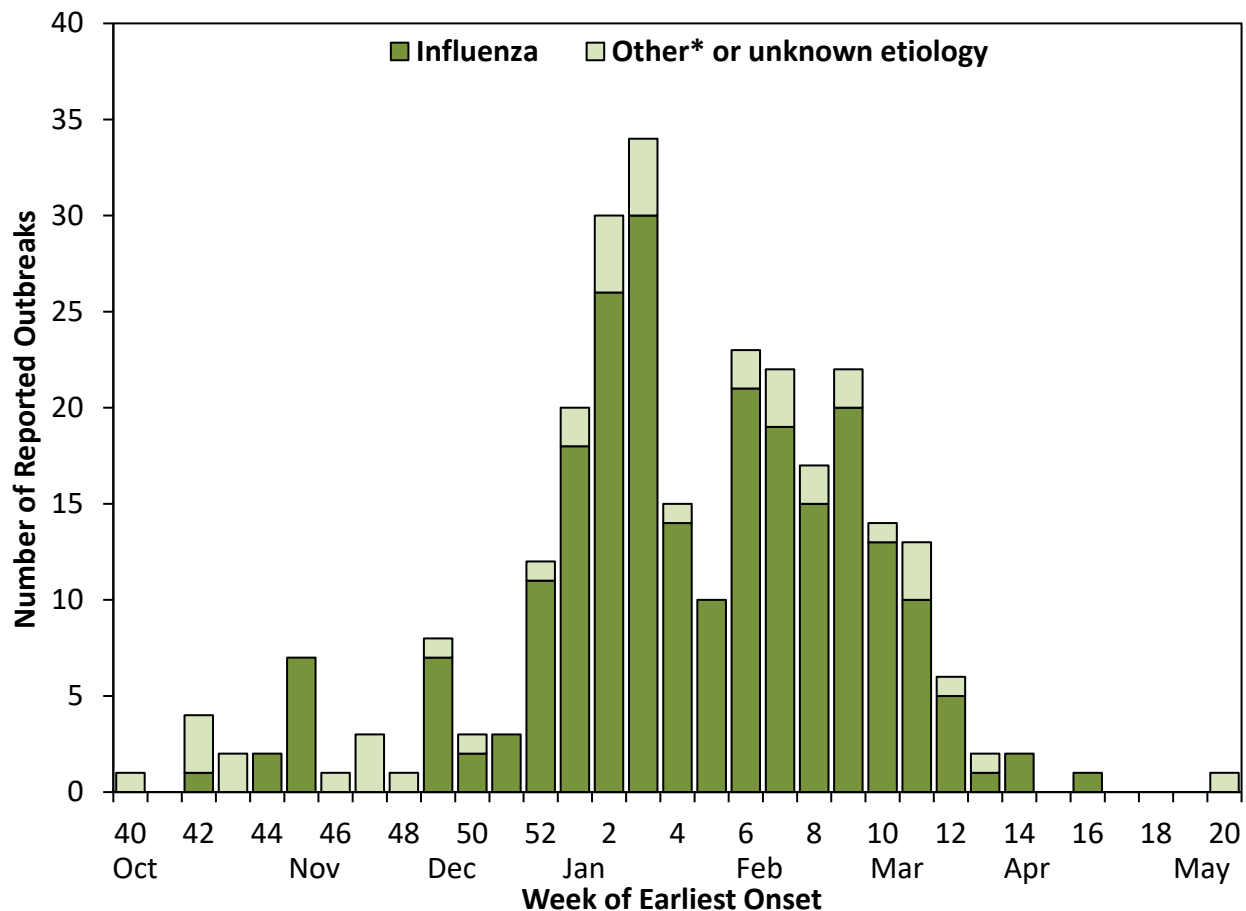
Outbreaks are required to be reported to the local health authority under Title 17, CCR 2500; however, outbreaks occurring in residential care facilities are more likely to be identified and reported to CDPH than other respiratory outbreaks. In general, respiratory, non-tuberculosis outbreaks are defined as a sudden increase of acute respiratory illnesses over the normal background rate.

From September 29, 2019 to May 16, 2020 local health departments reported a total of 279 confirmed non-tuberculosis and non-COVID-19 respiratory outbreaks to the CDPH. The outbreaks were reported from 36 local health jurisdictions throughout the state. Of the 279 confirmed respiratory outbreaks, influenza was the most commonly identified pathogen (238; 85.3%). Twenty (7.2%) confirmed respiratory outbreaks had no identified etiology. The remaining 21 (7.5%) outbreaks identified RSV (6), rhinovirus (5), mumps (4), pertussis (3), Group A streptococcal infection (2), and non-SARS-CoV-2 coronavirus (1).

The first influenza-associated outbreak identified during the 2019–2020 influenza season occurred in mid-October 2019 (Figure 18). Influenza outbreaks continued to occur through mid-April, with peak activity occurring in during mid-January. No confirmed influenza outbreaks were reported to the CDPH with initial case onset during the weeks ending May 23, 2020 through September 26, 2020.

Of the 238 influenza-associated outbreaks, 175 (73.5%) were associated with influenza A and 19 (8.0%) were associated with influenza B, and 22 (9.2%) were associated with both influenza A and influenza B. An additional 22 (9.2%) outbreaks were associated with influenza, but the influenza type was not known. Of the 197 outbreaks where influenza A viruses were identified, 22 (11.2%) had subtyping information available; 3 (13.6%) were A (H3N2), and 19 (86.4%) were A (H1N1)pdm09. Of the 41 outbreaks where influenza B viruses were identified, 4 (9.8%) had lineage typing performed; four (100%) were B/Victoria lineage. Most influenza A (175; 88.8%) and influenza B (37; 90.2%) specimens were not subtyped or lineage typed.

Of the 238 influenza-associated outbreaks, 161 (67.6%) occurred in residential healthcare facilities, such as skilled nursing facilities, and 36 (15.1%) occurred in assisted or independent living facilities (congregate residential facilities not providing routine healthcare). Local health departments also reported influenza outbreaks in schools or colleges/universities (14; 5.9%), correctional facilities (16; 6.7%), acute care facilities (2; 0.8%), and other medical facilities (4; 1.7%). Five (2.1%) occurred in other settings.

Figure 18. Reported respiratory outbreaks by week of earliest onset, September 29, 2019–May 16, 2020

* Other etiologies identified by laboratory confirmation included RSV (6), rhinovirus (5), mumps (4), pertussis (3), Group A streptococcal infection (2), and non-SARS-CoV-2 coronavirus (1).

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⁵ Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2018–19 influenza season. Morb Mortal Wkly Rep. 2018 Aug 24; 67(RR-3);1-20.

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[Back to top of report](#)